Global Regulatory Policy

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Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: 04D-0465 Draft Guidance for Industry; Chemical, Manufacturing, and Control Information for Human Gene Therapy Investigational New Drug Applications

Merck & Co., Inc. is a leading worldwide human health product company. Merck's corporate strategy — to discover new medicines through breakthrough research — encourages us to spend nearly $3 billion annually on worldwide Research and Development (R&D). Through a combination of the best science and state-of-the-art medicine, Merck's R&D pipeline has produced many of the important pharmaceutical and biological products on the market today.

Merck Research Laboratories (MRL), Merck's research division, is one of the leading U.S. biomedical research organizations. MRL tests many compounds as potential drug candidates through comprehensive, state-of-the-art R&D programs. Merck supports regulatory oversight of product development that is based on sound scientific principles and good medical judgment. In the course of developing products to treat and prevent a variety of diseases, Merck scientists regularly address issues affected by the draft guidance (hereafter referred to as the Guidance). Therefore, we are well qualified to comment on this guidance

Overall, Merck applauds the FDA's efforts to enhance the IND review process. Specifically, we commend the Agency for allowing the use of newer methods for the detection of adventitious agents and analytical characterization. Below, we have identified sections in the draft guidance for which we have provided comments that seek to help the Agency in its efforts.

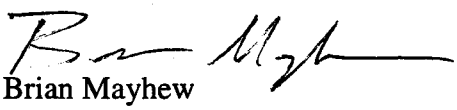
Recommendations

Section III.A.2.b. Cell Bank System, page 6
Merck believes that the Agency's final guidance should acknowledge that, for programs that are early in development or perhaps some special types of products (e.g., autologous dendritic cell therapies), it may not be justifiable or feasible to prepare a two-tiered banking system and that in such cases a Master Cell Bank and, if applicable, a Master Viral Bank would be sufficient to support clinical investigation. While we understand the FDA is not mandating two-tiered systems, it may be inferred from this section and therefore, we recommend that the FDA state explicitly that exceptions to a two-tiered cell banking system may be justifiable on a case-by-case basis.

Section VII.E. Qualification of the Manufacturing Process, page 26
In the third sentence of the third paragraph, the guidance states "most gene therapy products are not subject to final sterile filtration" and as such the FDA suggests that these products be manufactured under asceptic processing. Merck believes that the section might lead sponsors to use and reviewers to require asceptic processing even in cases where asceptic processing is unnecessary. Therefore, Merck recommends that the FDA reword the guidance to the following:
"We suggest that products that are not subjected to a processing step that helps to ensure sterility, such as a final sterile filtration, be manufactured under asceptic conditions."

In conclusion, MRL applauds the FDA's continuing efforts to enhance the preparation and review of the IND process. We welcome the opportunity to comment on this draft Guidance and to meet with you to discuss our comments. Please feel free to contact me at (301) 941-1402.

Sincerely,



Brian Mayhew
U.S. Regulatory Policy